REMARKS

Status of the Claims

Claims 25, 26, and 28 have been amended. Claims 1-24, 27, 29-36 have been canceled without prejudice or disclaimer of the subject matter contained therein. The amendments to the claims do not introduce new matter.

Rejection under 35 U.S.C. 112, first paragraph

Claims 25, 26, 28, and 31-36 were rejected under 35 U.S.C. 112, first paragraph, for allegedly failing to comply with the written description requirement. The crux of the rejection is that the specification allegedly does not provide adequate written description for the claimed genus. Applicants respectfully disagree. Contrary to the allegations in the Office Action, the specification clearly provides written description for anti-human CXCR4 antibodies that function (a) to inhibit the binding between the ligand human SDF-1 and the receptor human CXCR4 and (b) to treat a solid tumor, to treat a disease pathologically caused by neovascularization or suppress vascularization as claimed.

Applicants submit that the claimed invention is disclosed in the specification. Applicants hereby reiterate all previously presented arguments, and again point out that support for the claimed invention is found throughout the specification. The production of antibodies to a known antigen is a rudimentary process achievable by a skilled artisan so long as the antigen is fully described. To that end, the specification discloses the amino acid and nucleotides sequences of human CXCR4 (SEQ ID NO: 1) (page 14, lines 24 to 26). The specification further describes at least:

i. that both SDF-1 and CXCR4 are necessary for neovascularization (page 2, line 20 to page 4, line 10);
ii. the structural of details of CXCR4 (page 2, line 20 to page 4, line 10);
iii. the role of SDF-1 (page 2, line 20 to page 4, line 10);
iv. anti-CXCR4 antibodies (page 18, lines 10 to 11);
v. how to make such anti-CXCR4 antibodies (page 26, line 25 to page 32, line 36); and
vi. methods of treating cancer, treating a pathology caused by neovascularization, and suppressing vascularization with such antibodies (*see* page 38, lines 15 to 25).

Accordingly, the specification discloses the full sequence and the structure of the antigen, as well as antibodies that bind to the antigen and methods of making such antibodies. Each element of the claims is disclosed in the specification and one of skill in the art would recognize what is claimed in sufficient detail to reasonably conclude that the inventors were in possession of the claimed invention (*see* MPEP 2163).

As further evidence, Applicants submit with this response the reference of Forster (J. Immunol. 160: 1522-1531, 1998), which discloses evidence of antibodies that bind to CXCR4 and thereby inhibit a downstream HIV-1 infection. As evidenced by Crump (EMBO J. 16: 6996-7007, 1997, attached hereto), CXCR4 functions as a corecpetor for HIV-1, and HIV-1 inhibits SDF-1 from binding to CXCR4. Thus it is apparent that the HIV-1 binding site on CXCR4 shares the SDF-1 binding site. Therefore, inhibiting HIV-1 binding with an antibody will also inhibit the binding of SDF-1. The methods of Forster recite routine production of antibodies using techniques well known in the art at the time of the present application. As such, Forster demonstrates production of antibodies that inhibit the binding of SDF-1 to CXCR4 through the starting point of simply knowing the antigen. The specification in combination with Forster, therefore, demonstrates to one of ordinary skill in the art that Applicants were in possession pf the claimed invention.

Applicants previous response pointed to support from similar cases supporting the notion that full disclosure of the antigen provides adequate written description for an antibody against the antigen. *Noelle v. Lederman*, 355 F.3d 1343, 1349 (Fed. Cir. 2003) states that "as long as an applicant has a '*fully characterized* antigen' by its structure, formula, chemical name, or by depositing the protein in a public depository, the applicant can then claim an antibody by its binding affinity to that described antigen." Further, Applicants respectfully point out that there is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed. *In re Wertheim*, 541 F.2d 257, 262, (CCPA 1976). Accordingly, as the specification has fully characterized the antigen, as well as the interaction between the ligand and receptor, an antibody claimed by its binding affinity is described.

The Examiner appears to refute this rule of law with the nuanced assertion that antibodies that inhibit the binding of SDF-1 and treat a tumor, a disease pathologically caused by neovascularization, or suppressing vascularization are not described. The Examiner alleges that such treatments are not routine. Applicants respectfully disagree. All of the claims are directed to inhibiting SDF-1 from binding to CXCR4 by blocking the binding site for SDF-1 with an antibody. As discussed above, and as demonstrated by Forster, such antibodies are produced routinely once the full antigen is known. The Examiner has raised no objection to the fact that the antigen is fully described. The downstream vascularization consequences of SDF-1 binding to CXCR4 are described, and as such, inhibiting the vascularization signaling cascades turned on by the interaction between SDF-1 and CXCR4 by preventing SDF-1 binding are consequences of the antibody binding.

Further, with regard to *In re Alonso*, the Examiner refutes Applicants' previous arguments that this decision is inapplicable, as Applicants have not produced one species of antibody. Applicants submit that production of an antibody is not required for evidence of adequate written description. As found in *Noelle*, description of a full antigen is sufficient for describing antibodies directed against it. Applicants

respectfully point out that MPEP 2163.07(a) states that by disclosing in a patent application a device (*i.e.* antibody) that inherently performs a function or has a property, operates according to a theory or has an advantage (*i.e.* blocking the interaction between SDF-1 and CXCR4), a patent application necessarily discloses that function, theory or advantage, even though it says nothing explicit concerning it. Accordingly, by disclosing the interaction between SDF-1 and CXCR4 and antibodies to those proteins, the inherent function of blocking the interaction with an antibody is described.

Applicants previous response also did not fail to address the Examiner's points regarding *Lilly* and *Enzo*, but instead pointed to more relevant case law, namely *Noelle*. *Lilly* and *Enzo* concerned issues regarding the DNA sequences not being disclosed. *Noelle*, a later issued decision by the Federal Circuit, clearly states that antibodies derived from a fully disclosed antigen are satisfied for purposes of written description, thereby nullifying any applicability of *Lilly* and *Enzo*, which do not concern antibodies. Similarly, the Examiner's reliance of *Rochester v. Searle*, 358 F.3d 916 (Fed. Cir. 2004), is not applicable to the claimed invention. *Rochester* concerned claiming small chemical compounds to inhibit the activity of a prostaglandin H synthase-2 (PGHS-2) when such compounds had not been identified. However, antibodies are well known compounds in the art, and can be readily produced. It appears as though the Examiner is applying *Rochester* for the notion that a variable domain on an antibody had not been identified. This is very different from a completely theoretical compound that could comprise any number of molecules and could be of any size. Antibodies, unlike the issues in *Rochester*, are well described, characterized and understood in the art. Unlike *Rochester*, one skilled in the art can immediately recognize how to make and produce the claimed invention based on the specification.

In summary, Applicants submit that the specification fully demonstrates to one of skill in the art that that Applicants were in possession of the claimed invention as a whole at the time of filing. As demonstrated by Forster, antibodies interrupting SDF-1 binding to CXCR4 have been found through routine experiments as described in the specification (*see* page 26, line 25 to page 32, line 36). The disclosure of a full antigen is present in the specification and is legally sufficient to satisfy the written description requirement. *See Noelle v. Lederman*, 355 F.3d 1343 (Fed. Cir. 2003). Moreover, the specification describes the interaction between SDF-1 and CXCR4, as well as antibodies to these proteins, thereby inherently describing the activity of antibodies to blocking the interaction. MPEP 2163.07(a).

Conclusion

It is respectfully submitted that all claims are now in condition for allowance, early notice of which would be appreciated. Should the Examiner disagree, Applicants respectfully request a telephonic or in-person interview with the undersigned attorney to discuss any remaining issues and to expedite the eventual allowance of the claims.

If there are any additional fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,
Morgan, Lewis & Bockius LLP

/Zachary Derbyshire/
Zachary Derbyshire
Registration No. 64,669

Dated: **October 12, 2010**
Morgan, Lewis & Bockius LLP
Customer No. **09629**
1111 Pennsylvania Avenue, N.W.
Washington, D.C. 20004
202-739-3000